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THE VARIETIES OF PNEUMOCOCCI CAUSING LOBAR PNEUMONIA, WITH ESPECIAL REFERENCE TO THEIR BIOLOGIC DIFFERENCES *

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REACTIONS OF AGGLUTINATION

Experimental evidence now at hand indicates that during the course of lobar pneumonia there is a definite biologic reaction characterized by the formation of antipneumococcic substances in the body of the patient. These antibodies are of primary importance in bringing about a favorable termination of the disease. Attempts to utilize this fact in the treatment of pneumococcal infections have led to the important observation that pneumococci vary widely in their serologic reactions.

Eyre and Washbourn[1] found that a given antipneumococcic serum would protect rabbits only against certain strains of pneumococci. Bezançon and Griffon[2] confirmed this observation by experiments in both agglutination and protection. The researches of Neufeld and Händel[3] indicate that pneumococci might be classified into different groups according to their biologic differences, and the practical application of this principle was made by Dochez and Gillespie[4] in America and Lister[5] in South Africa.

Dochez and Gillespie found that pneumococci obtained from cases of pneumonia could be classified into 4 groups according to their biologic and cultural differences. A highly immune serum was prepared for each of 2 groups (I and II) and all the organisms not affected by these sera, except pneumococcus types (Group III), were placed in an atypical group (IV). These observers found that the most common type of organism in New York City during the season of 1912-13 was that of Group I. In 1913-14 the percentage incidence of the typical groups (I and II) did not change, but Group II became the dominant type.[6]

A similar study has been made of the cases of lobar pneumonia entering the Cook County Hospital during the season of 1914-15, the results of which are recorded in this paper. I am greatly indebted to the members of the medical staff of the Cook County Hospital for the clinical material so willingly placed at my disposal.

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[1] British Med. Jour., 1899, 2, p. 1247.
[2] Ann. de l'Inst. Pasteur, 1900, 14, p. 449.
[3] Arb. a. d. k. Gsndhsamte., 1910, 34, p. 293.
[4] Jour. Am. Med. Assn., 1913, 61, p. 727.
[5] Specific Serologic Reactions with Pneumococci from Different Sources, 1913.
[6] Jour. Exper. Med., 1915, 21, p. 114.

TECHNIC

Blood cultures were made in the usual manner. A mixture of 3-5 c.c. of blood with 100 c.c. of plain broth (0.7% acidity to phenolphthalein) was incubated for from 1 to 6 days at 37 C. Sputum cultures were made according to a method advised by Cole and Dochez.[7] A small amount of sputum was obtained by having the patient cough and expectorate into a wide-mouthed bottle or Petri dish. A small particle of this sputum, thoroughly washed, was ground up in a sterile mortar with 12 c.c. of normal salt solution or plain broth and this mixture injected into the peritoneal cavity of a mouse. The mouse was killed in from 6 to 24 hours and cultures made from the heart's blood and the peritoneal exudate. Whenever enough time had elapsed after inoculation (18-24 hr.), a pure culture of pneumococci was usually obtained from the blood, as well as from the peritoneal exudate. Smears of the ground sputum on blood agar plates usually gave a luxuriant growth of pneumococci. Since only typical cases of lobar pneumonia were studied, the identification of the organism in subcultures was not difficult. All grades of variation, however, were encountered in the different cultural reactions.

Bacteriologic examination was made in 142 cases of acute lobar pneumonia during the active stage of the infection. In 128 of the cases blood cultures were made, in 97 or 75% of which the pneumococcus was isolated in pure culture. In 31 instances the blood cultures were negative, but in many of these the blood was examined late in the course of the infection. Usually the blood cultures were positive in from 24 to 48 hours; in a few it required from 4 to 6 days for an appreciable growth to take place. This was especially noticeable in the cultures obtained after the fifth day of the disease, and was probably due to the marked decrease at this time in the number of organisms in the blood. In 6 cases both the blood and sputum were examined, similar organisms being obtained from both sources. Of the remaining 14 cases, the sputum alone was examined. The organisms were typical pneumococci, in most instances, and highly virulent, as evidenced by the rapidity with which the mouse became ill after inoculation. The organisms often invaded the blood within 18 hours. When plate cultures were made, 2 types of pneumococci were sometimes isolated, which, in a few instances, could be differentiated by their cultural differences on blood agar plates. This discrepancy between the plates and the mouse cultures may be explained by assuming that the avirulent organisms are overgrown in the peritoneal cavity of the mouse by a more virulent strain. The characteristic inulin reaction was present in almost all instances in which the organism was studied early after isolation; this acid-forming power decreased however with the continued growth of the organism on artificial media. A few of the strains of pneumococci, with continued growth on blood agar, have become slightly hemolytic.

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[7] Personal communication.

AGGLUTINATION TESTS

The technic used in these tests was similar to that used by Cole (to whom I am indebted for specific sera of Groups I and II with marked agglutinative powers) and his associates. Equal parts of a suspension of the pneumococci in normal salt solution and the sera of Groups I and II were mixed in small test tubes. The mixtures were incubated at 37 C. for 2 hours and if agglutination was not complete at the end of this time they were placed in the refrigerator for 24 hours before a final result was recorded. Agglutination often occurred within the first hour; a negative reaction, however, could only be determined after a period of 24 hours. Each strain of pneumococcus was studied by these methods as soon after isolation as possible. When there was partial agglutination with both sera, varying dilutions of each serum were used in the tests. The results of the tests are recorded in Table 1.

TABLE 1

BIOLOGIC CLASSIFICATION OF THE DIFFERENT STRAINS OF PNEUMOCOCCI AS DETERMINED BY THEIR REACTIONS OF AGGLUTINATION

Group	No. of Cases	Percentage of Total
I	50	45.0
II	25	22.5
III	5	4.5
IV	31	28.0

Of the 111 strains of pneumococci studied, 50 were found to belong to Group I, 25 to Group II, and 5 strains were typical members of the pneumococcus mucosus group. The remaining 31 strains, atypical in their biologic reactions, were considered as members of Group IV, or the heterologous group.

The members of Group I comprised 45% of the total number of cases. With the organisms of Group I the agglutination was very striking, taking place usually in a very short time. In 22.5% of the cases an organism belonging to Group II was isolated. With these organisms the agglutination was less striking than with the members of Group I, and often little change could be detected in the mixtures after 2 hours' incubation. In most instances it required 24 hours for the reaction to take place.

There were 31 atypical strains of pneumococci that could not be classified biologically or culturally. Many of these organisms were partially agglutinated by both Sera I and II. In some instances the action was more pronounced with one than with the other. When the organism was partially agglutinated by both sera, different dilutions of the sera were used. Usually little was gained by this procedure, for agglutination disappeared in very low dilutions. In two instances (Strains 134 and 143), however, the organisms were partially agglutinated by both sera dilutions as high as 1 : 128. It is interesting to note at this point that the typical members of Groups I and II are usually not agglutinated by their homologous sera in high dilutions. Fifteen of the 31 organisms of the heterologous group were not agglutinated by either of the specific sera.

In Types I, II, and IV the morphology was practically the same. Variations in size, shape, and arrangement of the organisms were as frequent in one of these groups as the other. Culturally, however, the members of Group II gave usually a more moist growth than did those of Group I, but the capsules were not appreciably larger. Organisms of the mucosus type produced abundant mucus on blood agar plates; they were uniformly small, surrounded by a heavy capsule. The biologic characteristics of the strains of pneumococci grown on artificial media since their isolation have not varied.

MORTALITY

The cultures were made on early cases of lobar pneumonia without regard to age or any other factor which influences mortality—a few of the cases being moribund at the time cultures were taken. In Table 2 the mortality for each group is recorded. Thirty-eight of the 142 cases resulted fatally,—a mortality of 26.7%. The lowest mortality was in Groups I and IV. In Group II the mortality was somewhat higher, and in Group III, 80% of the cases terminated fatally. In the cases in which negative blood cultures were obtained, the death rate was small (19.3%) ; this supports the view that in favorable cases the organisms disappear from the blood early in the course of the infection.

TABLE 2
THE RELATION OF THE BIOLOGIC DIFFERENCES OF PNEUMOCOCCI TO MORTALITY

Group	Recovered	Dead	Mortality
I	37	13	26.0%
II	18	7	28.0%
III	1	4	80.0%
IV	23	8	25.8%
Negative cultures	25	6	19.3%
Total	104	38	26.7%

The relation of age to the incidence and mortality of lobar pneumonia is shown in Table 3. Young, healthy adults between the ages of 20 and 40 years are most often infected. The mortality is strikingly low during the first three decades, but increases greatly with each succeeding decade.

The severity of the course and the clinical picture varied in all the groups, so that there were no clinical observations that could be considered peculiar to one single group. Usually, however, in the Group I series the clinical picture was relatively typical, and a crisis was more common than lysis when there was a favorable termination. Complications were not uncommon, and a few individuals suffered two attacks of pneumonia at short intervals. In one of these cases a careful bacteriologic study was made, the findings of which were of sufficient interest to report.

TABLE 3
THE RELATION OF AGE TO THE MORTALITY IN LOBAR PNEUMONIA

Decade	Recovered	Dead	Mortality
10-20	5	0	0
20-30	34	2	5%
30-40	36	15	29%
40-50	16	12	42%
50-60	9	6	40%
60-70	4	3	43%
Total	104	38	26.7%

TWO ATTACKS OF LOBAR PNEUMONIA IN THE SAME INDIVIDUAL, CAUSED BY PNEUMOCOCCI WITH DIFFERENT IMMUNOLOGIC REACTIONS

A second attack of lobar pneumonia in the same individual is not an uncommon occurrence in hospital practice. While the symptoms of the first attack are abating and recovery seems assured, the patient suddenly develops a chill and another typical pneumonia ensues. In the absence of contradictory evidence the natural supposition has been that both infections are caused by the same organism. Other possibilities, however, must be considered. Is such an occurrence a new infection by a different organism, or a variation of the organism causing the first infection? Or may it be a latent process activated by the debilitating effects of the first attack? The following incidence of such an infection is important in this connection:

CASE 68.—A laborer 56 years of age, in the medical service of Dr. Capps and Dr. Post, entered the Cook County Hospital, Feb. 6, 1915, complaining of a severe cough, high fever, and pain in the right side of the chest. His sickness had begun the day before with headache and a cough. These symptoms

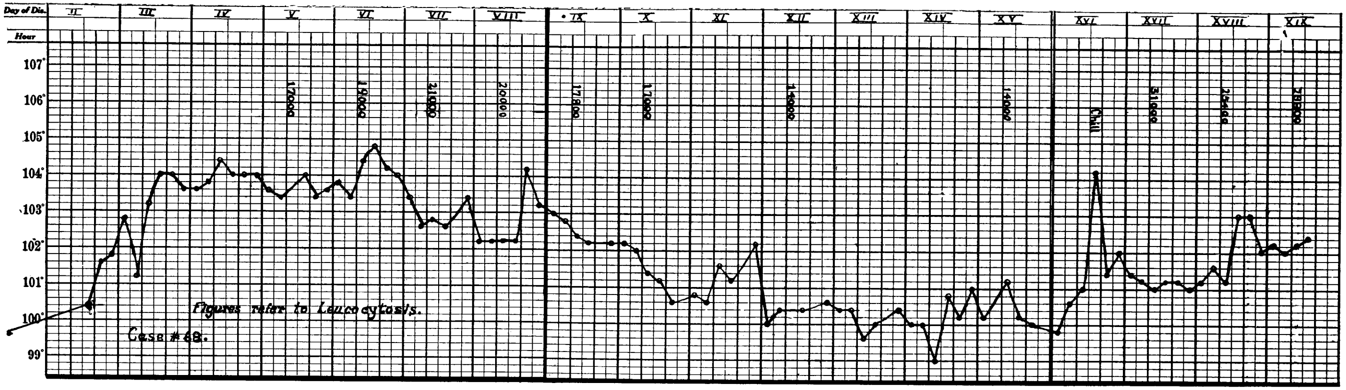

Chart 1.—The temperature and leukocytes in the case of two attacks of pneumonia in the same individual.

had rapidly increased and he had had a severe chill a few hours before his entrance into the hospital. Following the chill all the subjective signs of a lobar pneumonia appeared. With the exception of a chancre 20 years before, the remainder of the history is unimportant.

He was well nourished. His respirations were rapid, shallow, and painful. The throat and tonsils were reddened. On the right side of the chest, at the level of the fourth interspace anteriorly, and at the angle of the scapula posteriorly, there were areas of dullness, bronchial breathing, and bronchophony. Over the remainder of the right chest, the breath sounds were distant; numerous moist râles were to be heard throughout respiration. The left lung was unchanged. The left border of the heart was 11 cm. to the left of the midsternal line; the heart sounds were regular and clear, without audible murmurs. At the time of this examination the temperature was 104 F., pulse 98, and respiration 48. The sputum was thin, blood-tinged, and stained smears revealed numerous gram-positive, encapsulated diplococci. There was a polymorphonuclear leukocytosis of 17,000 per c.mm. The urine was normal, except for a decreased chlorid content. The systolic blood pressure was 85 mm. and the diastolic 65 mm. of mercury.

All the signs and symptoms of an acute lobar pneumonia involving the right middle and lower lobes of the lung intervened (see Chart 1); the course was severe and the patient, delirous. On the sixth day an acute, purulent arthritis of the left shoulder developed. The joint was drained 3 days later, a thick, yellow, purulent material being obtained from which a pneumococcus was isolated in pure culture. The temperature began to fall by lysis on the seventh day. The symptoms rapidly abated and by the twelfth day resolution was in progress and the temperature was 99 F. per rectum. The patient felt fairly well until the fourteenth day, when he suddenly had a violent chill while all the symptoms and signs of a lobar pneumonia involving the lower left lobe of the lung intervened. Respirations increased from 24 to 56; the leukocytes from 14,000 to 31,000 per c.mm. The symptoms rapidly increased and the patient died Feb. 23, 1915.

Anatomic Diagnosis (Dr. Herzog).—Lobar pneumonia of both sides, with red and gray hepatization; fatty and parenchymatous degeneration of the myocardium; marked dilatation of the right side of the heart; parenchymatous degeneration and fatty changes of the liver; passive hyperemia of the kidneys; metastatic purulent arthritis of the left shoulder.

Bacteriologic Examination.—Typical pneumococci were isolated from the blood in 3 different instances,—on the third and fourth days of the first attack, and on the third day of the second attack. Pneumococci were isolated also from the purulent material from the infected shoulder joint and the sputum. The organisms were all similar morphologically and culturally but different in their reactions of agglutination. The blood cultures made during the primary infection, and the culture made from the joint, yielded an organism which was agglutinated by the serum of Group I. The organism isolated from the blood and sputum during the second attack was not agglutinated by either the serum of Group I or that of Group II. Morphologically, however, the organisms were similar. On blood agar plates the colonies were green-colored and slightly more moist than those of the first infection. Both organisms were encapsulated, and in their cultural reactions typical of the pneumococcus group.

In this case there were two different pneumococcus infections caused by organisms with different biologic reactions. The first infection was caused by an organism with the biologic characteristics of Group I; the terminal infection was caused by a member of the heterologous group. Was this new organism derived from the external world, or was it a variation of the pneumococcus already present in the body in large numbers? The latter explanation seems the more probable, for in the body of an individual suffering from lobar pneumonia the environmental conditions are ideal for a change in the biologic characteristics of the invading pneumococcus. Rosenow[8] has shown that these biologic reactions may change under experimental conditions. By varying the media on which pneumococci are grown, cross agglutination between Groups I and II can be obtained. Hence, if these observations are correct, it seems reasonable to assume that the same organism may be the causative factor in both infections, the immunity perhaps being overcome, as suggested, by a change in the biologic reaction of the pneumococcus.

SUMMARY

The pneumococci isolated from the blood and the sputum of patients suffering from lobar pneumonia vary widely in their biologic reactions. By means of agglutination tests with specific immune sera, these pneumococci may be classified into certain biologic groups. There are many atypical organisms, however, exhibiting the biologic characters of both groups to a limited extent. With the exception of the pneumococcus mucosus type, these different groups have no distinguishing morphologic or cultural peculiarities. Group I is the most typical group, but its members are less virulent than those of Groups II and III. Group IV is the least virulent of the four types.

During the winter of 1914-15 the percentage incidence of the typical groups (I, II, and III) in the vicinity of Chicago was 72%, and 28% for the heterologous types (Group IV). These figures are approximately the same as those obtained by Dochez and Avery in New York city during the two preceding seasons. Group I was the dominant type, and Group IV was more frequent than Group II or III. This predominance of the less virulent groups (I and IV) is again indicated by the very low mortality (26.7%) for the series.

Repeated attacks of pneumonia occurring at short intervals in the same individual may be caused by pneumococci with different biologic reactions.

[8] Jour. Infect. Dis., 1914, 14, p. 1.